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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/027,671 02/23/98 SMITH

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KM  
EXAMINER

022850 HM22/0327  
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ART UNIT PAPER NUMBER

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No. 09/027,671	Applicant(s) AK Smith, et al.
	Examiner Mary B. Tung	Group Art Unit 1644

Responsive to communication(s) filed on Jan 12, 2001

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claim

- Claim(s) 6-12, 15-32, and 38-47 is/are pending in the application.  
 Of the above, claim(s) 15-32 is/are withdrawn from consideration.  
 Claim(s) \_\_\_\_\_ is/are allowed.  
 Claim(s) 6-12 and 38-47 is/are rejected.  
 Claim(s) \_\_\_\_\_ is/are objected to.  
 Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.  
 The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.  
 The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.  
 The specification is objected to by the Examiner.  
 The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).  
 All  Some\*  None of the CERTIFIED copies of the priority documents have been  
 received.  
 received in Application No. (Series Code/Serial Number) \_\_\_\_\_  
 received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- Notice of References Cited, PTO-892  
 Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_  
 Interview Summary, PTO-413  
 Notice of Draftsperson's Patent Drawing Review, PTO-948  
 Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

***DETAILED ACTION***

1. Claims 1-5, 13, 14 and 33-37 were cancelled in the paper filed 1/3/2001, Paper No. 17.
2. Claims 46 and 47 were added in Paper No. 17.

***Election/Restriction***

3. Claims 15-32 stand withdrawn from further consideration by the Examiner, 37 C.F.R. 1.142(b), as being drawn to non-elected inventions.

***Claim Rejections - 35 U.S.C. § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 6, 9-12 and 38-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Kraus (US Patent 5,674,750).

6. The '750 patent teaches a method for obtaining lineage committed hematopoietic stem cells by replacement of culture medium with enhanced proliferative potential, (proliferative and replicative potential, as recited in claim 12 is known in the art as equivalent to clonogenic expansion, see col. 1 and col. 2, lines 58 and bridging over to col. 3, line 18), wherein the cells are cultured for at least 2 days, as recited in claim 10 (more than 5 days, see col. 12), wherein the medium contains at least one growth factor which stimulates the proliferation of the cells, as recited in claim 11 (see col. 8, lines 31-36), having enhanced biological function, as recited in claims 38 and 39 (the definition of biological function includes the ability to proliferate to development and regeneration of tissue similar to naturally occurring structure and function on page 11 of the specification, see col. 9), and wherein the lineage committed cells comprise hematopoietic and myeloid precursors, (see col. 1, lines 9-13 and col. 2, line 66 and 67), as recited in claim 43. The '750 patent also teaches lymphoid precursors (see col. 2, line 67), which would inherently comprise T cells or dendritic cells, as recited in claims 6, 44 and 45 (see also col. 3, lines 55 and 56, wherein the cell surface markers include T cell and dendritic cell markers, such as CD19, CD33, CD38 and HLA-Dr, as evidenced by Ager, et al. (*Immunology Today 2nd ed. The Immune Receptor Supplement 1997, 2nd Ed. Elsevier Trends Journals, Cambridge, UK*)). The recitation of claims 40 and 41 wherein the lineage committed cells comprises the increased

release of cytokines and increased cytolytic activity would be inherent in the proliferation of myeloid and CD19+, CD33+ and CD38+ cell population taught by the '750 patent, because an increased proliferation inherently induces an increase in cytokines and the CD19+, CD33+ and CD38+ would inherently contain cytotoxic T cell precursors. The '750 patent also teaches that the cells are human, as recited in claim 6 (see Figure 5). The cells of the '750 patent are inherently cultured, as recited in claim 6. Therefore, the reference teachings anticipate the claimed invention.

Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the Applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. *In re Schreiber*, 44 USPQ2d 1429 (Fed. Cir. 1997).

7. Applicant's arguments filed in Paper No. 17 have been fully considered but they are not persuasive.
8. Applicants argue that "**Kraus** do not disclose the present method of obtaining **lineage committed human cells having enhanced biological function** as recited in Claim 1" [emphasis added by Applicants] This argument is not found persuasive, however, because Claim 43 lists hematopoietic cells and mesenchymal cells as lineage committed cells. Mesenchymal stem cells are known in the art as stem cells, which give rise to various cell types, such as bone, muscle, and so forth. Therefore, given the recitation of hematopoietic cells in claim 43, the HSCs taught in Kraus would clearly be within the scope of stem cells that give rise to multiple cell types, as are the recited mesenchymal stem cells. The argument is also not found persuasive because Kraus, et al. teach the enhancement of biological function, as discussed, *supra*. Hematopoietic stem cells are committed to myeloid and non-myeloid lineages, and thus are encompassed by the definition of "lineage specific." The argument on page 5 of the response that "the cells.... are differentiated at least to the point where they are programmed to develop into a specific cell" also is encompassed by the Kraus reference, since the Applicants also state on page 7, lines 4-5 of the specification that "the lineage committed cells are more differentiated than human stem cells" absent a clear definition of "human stem cells" which broadly would encompass embryonic or pluripotent stem cells. Also, the '750 patent teaches selecting and expanding a differentiated pool of cells (see col. 2, line 58 and bridging over to col. 3, line 5 and col. 9, line 63 and bridging over to col. 10, line 3). The definition of biological function includes the ability to proliferate to development and regeneration of tissue similar to naturally occurring structure and function on page 11 of the specification, (see col. 1, lines 18-26, col. 2, lines 42-49 and col. 9 lines 53-62). Kraus therefore, by teaching a population of cells which would provide a population of cells which would regenerate a tissue (bone marrow) similar to naturally occurring structure and function would be encompassed by the claims.

***Claim Rejections - 35 U.S.C. § 103***

9. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 6-8, 38 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kraus (US Patent 5,674,750) in view of Schwartz, et al. (US Patent No. 5,728,581).

12. The '750 patent has been discussed as applied to claim 1, *supra*. The claimed invention differs from the reference teaching only by the recitation of the replacement of 50% of the medium per day. The '581 patent also teaches the expansion of hematopoietic stem cells. However, in order to allow expansion of the stem cells, the '581 patent teaches that the cell density is kept at an optimum (see col. 9, lines 1-11) and that the medium is exchanged at a rate of 0.25 (1/4) to one-half per day (see col. 8, lines 59-61) and that the cell numbers are  $10,000 (1 \times 10^4)$  to  $200,000 (2 \times 10^5)$  cells/ml (see col. 6, lines 28-44), which is well within the range cited in claim 8. One of ordinary skill in the art at the time the invention was made would have been motivated to keep the cell density at an optimum and to change of the medium per day, as taught by the '581 patent in the method taught by the '750 patent, in order to allow the expansion of the stem cells. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. The response to the Applicants' arguments concerning the Kraus et al. reference was discussed, *supra*. Applicants additionally argue that Schwartz et al do not remedy these deficiencies because Schwartz et al merely teach a method of expanding hematopoietic

stem cells. The Applicants' assertions that the methods of Kraus and Schwartz would have a reduced biological activity as compared to the cells of the instant application is unsupported by factual evidence. The Applicants additionally argue that the cells produced by the recited methods would have a higher replicative potential. This argument is also not supported by factual evidence and is further not persuasive because the limitations are not present in the claims. The Applicants provide examples on pages 6 and 7 of the response, from the specification of enhanced biological activities, but this argument is not found persuasive because these activities were not intended by Applicants to be exhaustive (see page 23, lines 1-12 of the specification). Also, the '750 patent teaches the potential of "generational" potential of one HCS that can produce  $50 \times 10^6$  progeny (see col. 1, lines 13-16), which would be well within the definition of high replicative potential, asserted by the Applicants. Therefore, the rejection is maintained.

### *Conclusion*

No claim is allowed.

14. This application contains claims 15-32, drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

16. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 305-3014 or (703) 308-4242.

18. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mary Tung whose telephone number is (703)308-9344.

The Examiner can normally be reached Monday through Friday from 8:30 am to 5:30 pm. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1640 receptionist whose telephone number is (703) 308-0196.

*David A. Saunders*

DAVID SAUNDERS  
PRIMARY EXAMINER  
ART UNIT 1644

*Mary B. Tung*  
March 23, 2001  
Mary B. Tung, Ph.D.  
Patent Examiner  
Group 1640